Epitomes

Important Advances in Clinical Medicine

Allergy and Immunology

The Council on Scientific Affairs of the California Medical Association presents the following inventory of items of progress in allergy and immunology. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome, and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, researchers, and scholars to stay abreast of these items of progress in allergy and immunology that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Allergy and Immunology of the California Medical Association, and the summaries were prepared under its direction.

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Food-Induced Anaphylaxis

FOOD-INDUCED ANAPHYLAXIS is a rare but dramatic and potentially fatal condition that occurs in patients with hypersensitivity to a food. Nearly all patients with food-induced anaphylaxis have had previous adverse reaction(s) to the food at fault. Anaphylactic reactions to a food are almost always immunoglobulin (Ig) E-mediated, and because of this, patients usually will have a positive skin-prick test unless they have recently taken antihistaminic drugs or are in a refractory state, which may last as long as two weeks after an anaphylactic episode.

Although there is no particular age or sex predilection for food-induced anaphylaxis, nearly all persons with this disorder are highly atopic, and many have a history of asthma that requires β_2-agonists or a history of eczema or allergic rhinitis. They often have many food allergies. In about 85% of the patients, the anaphylactic event occurs away from home, where there is less control over constituents and trace contaminants in the food or drink ingested. The foods most commonly causing a reaction in adults, in descending order, are peanuts, tree nuts, milk, eggs, shellfish, other fish, and miscellaneous foods including cereal grains, celery, and fruits. In early childhood, cow's milk and soy proteins are major allergens. Patients usually are not aware that the offending food has been ingested. Two common characteristics in many patients who die of food-induced anaphylaxis are denial of the severity of their food allergy and a reliance on oral antihistaminics alone to treat their symptoms.

Three clinical patterns that have been observed are uniphasic, biphasic, and protracted. About half of the patients have a uniphasic pattern. In severe uniphasic reactions, symptoms usually begin one to five minutes after ingestion of the offending agent. A sensation of itching and tingling in the mouth is followed by tightness of the throat, nausea, vomiting, and urticaria, progressing within 30 minutes to dyspnea, cyanosis, arrhythmias, hypotension, and shock. About a quarter of food-induced anaphylactic episodes are biphasic, with early oral and abdominal symptoms followed by an asymptomatic period of one to two hours, after which severe respiratory symptoms, hypotension, and shock may occur. In another quarter of episodes, patients have protracted cardiorespiratory symptoms requiring vasopressor medications and ventilatory support for more than 24 hours. A special form of food-induced anaphylaxis may occur in conjunction with exercise. In these cases, neither ingestion of the food nor exercise will, by itself, cause anaphylaxis. The reaction occurs during or immediately following exercise, but only if the offending food is ingested within a few hours before exercise takes place.

In most instances, the initial immunologic reaction occurs when food antigen binds to IgE antibodies attached to high-affinity receptors on sensitized mast cells. These cells are activated, causing the release of a host of biologically potent chemical mediators including histamine, leukotrienes, prostaglandins, bradykinin, platelet-activating factor, and others. The result is increased vascular permeability, edema, bronchial smooth muscle contraction, and peripheral vasodilation. Although IgE-mediated reactions account for most food-induced anaphylaxis, nonimmunologic or anaphylactoid reactions have been known to occur.

Most patients with anaphylactic reactions to a food have positive skin-prick tests to that food. Immunoglobulin E antibody tests are advantageous if a patient has dermographism, if the patient will be seen only during the anaphylactic or postanaphylactic period, or if there has been recent therapy with antihistaminics, all of which can invalidate skin tests. Intradermal skin tests and oral challenge tests should be avoided because of the danger of severe systemic reactions.

Prevention is the management of choice for food-in-

duced anaphylaxis. Patients should be warned in an unequivocal but considerate manner that they are at an increased risk for anaphylaxis and that death could result if instructions are not conscientiously followed. All foods to which the patient is allergic should be identified by careful history, skin-prick tests, and IgE antibody assays. Patients and parents should be taught to read labels and interpret lists of ingredients on packaged foods. Epinephrine and antihistaminics should be available at all times and should be given at the earliest sign of food-induced anaphylaxis. Epinephrine kits are available by prescription and should be available at child care locales and schools. As with any severe episode of anaphylaxis, life support measures may become necessary.

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Treatment of Human Immunodeficiency Virus Disease

TREATMENT OPTIONS for the spectrum of human immunodeficiency virus (HIV) disease and its complications continue to evolve. A goal of HIV disease management is to enhance or restore immune function. Although this has proved to be elusive, ongoing research appears promising for both active immunotherapy with vaccines, cytokine therapy, and ex vivo cellular expansion and passive immunotherapy with anti-HIV immunoglobulin infusions. Interferon alfa, an immune modulator approved for use in HIV-infected patients with Kaposi's sarcoma, is also under intensive investigation as an antiretroviral agent in combination with zidovudine.

The immune system may have less to battle if common and opportunistic infections can be prevented. This requires vaccination and prophylaxis. Preventive therapies for opportunistic infections continue to be an essential element of HIV disease management and the focus of intense research. Current recommendations include prophylaxis of *Pneumocystis carinii* pneumonia, *Mycobacterium avium* complex, and the use of preventive vaccines. The vaccines advocated include influenza, pneumococcal, hepatitis B, and routine childhood vaccines. It is recommended that the influenza vaccine be given yearly in October or November. The pneumococcal polysaccharide vaccine is recommended for all HIV-seropositive patients per the guidelines of the Centers for Disease Control and Prevention (CDC). Revaccination should be considered for patients having received the vaccine more than six years ago. Hepatitis B vaccine is advocated for all HIV-seropositive patients who are not immune (demonstrating antibody to core or surface protein) and who remain at risk for the hepatitis B virus. Recommendations for tetanus, mumps, rubella, and measles vaccination are the same as for patients without HIV disease. For patients traveling abroad, the recommendations are also the same as for persons without HIV, except for live vaccines (yellow fever, live oral polio, and live oral typhoid), which remain strictly contraindicated for all immunocompromised patients.

Pneumocystis carinii pneumonia prophylaxis is currently advocated for HIV-seropositive patients (primary prophylaxis) who have $CD4^+$ counts of less than 200×10^6 per liter (200 per μl) and any patient who has had *P carinii* pneumonia previously (secondary prophylaxis). Additional new indications include patients with constitutional symptoms such as oral candidiasis or unexplained fever for more than two weeks, regardless of the $CD4^+$ count. Clinical trials indicate the use of the combination product of trimethoprim and sulfamethoxazole to be superior to that of aerosolized pentamidine for preventing recurrent *P carinii* pneumonia (secondary prophylaxis); recent reports from the Eighth International AIDS Conference suggest that treatment with trimethoprimsulfamethoxazole is superior for primary prophylaxis as well. The recommended dose is one double-strength tablet per day. Alternative regimens include aerosolized pentamidine or dapsone.

Prophylaxis studies are being carried out for cytomegalovirus, *Cryptococcus neoformans, Toxoplasma gondii,* and other common opportunistic pathogens, and recommendations can be expected in the near future.

Primary tuberculosis, especially multiple drug-resistant tuberculosis, is a growing concern. *Mycobacterium tuberculosis* may be readily transmitted by the aerosol route, particularly during the administration of aerosolized pentamidine or other respiratory therapies. Consequently, it is now imperative to identify patients with active tuberculosis and to treat them rapidly and effectively. Tuberculosis testing is indicated for all HIV-seropositive patients; likewise, HIV testing is indicated for all persons with *M tuberculosis.* Skin testing with intermediate-strength purified protein derivative (PPD) is considered positive if there is 5 mm of induration. Anergy may cause the test to be falsely negative; therefore, concurrent controls with *Candida albicans,* tetanus toxoid, or mumps should be placed. Patients with a positive PPD should receive isoniazid prophylaxis for 12 months.

Prophylaxis for *Mycobacterium avium-intracellulare* is indicated for HIV-seropositive patients with CDC-defined acquired immunodeficiency syndrome (AIDS), particularly those with $CD4^+$ counts of less than 100×10^6 per liter. *M avium-intracellulare* is a possibly life-threatening opportunistic infection seen commonly in patients with AIDS. Estimates indicate that 30% to 50% of patients may be diagnosed with *M avium-intracellulare* within three years after their diagnosis of AIDS. Recently, rifabutin was approved for the prophylaxis of the disease; it has been well tolerated in clinical trials at the recommended dose of 300 mg a day. *M avium-intracellulare*